EXHIBIT B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 8 Cases*	

Expert Report of C. Bryce Bowling, MD, FACOG, FACS, FPMRS on Prolift/Prolift+M/Gynemesh

I. Credentials and Qualifications

My name is Chadwick Bryce Bowling. My curriculum vitae (CV) attached hereto as Exhibit A reflects my education, training and unique qualifications to render an opinion on Ethicon's Prolift/Prolift+M & Gynemesh. I am a Urogynecologist / Pelvic Reconstructive Surgeon. A "urogynecologist" is a gynecologist with advanced training and education in the evaluation and treatment of women with complex pelvic floor issues, including urinary and bowel incontinence complaints and pelvic prolapse/relaxation defects. I treat individuals with the above-mentioned problems, as well as those with pelvic pain syndromes, urinary and defecatory voiding dysfunction, interstitial cystitis, childbirth injuries, genital tract fistulas,

and I have extensive expertise in correcting serious mesh complications.

I am a *Summa Cum Laude* graduate of the University of Tennessee, Knoxville with a Bachelor in Sciences obtained in 1998. I obtained my MD from the University of Tennessee Health Sciences Center in Memphis, TN in 2003. I completed an internship and residency in Obstetrics & Gynecology at The Regional Medical Center in Memphis, where I served as Chief Resident. Following my residency in Obstetrics & Gynecology, I completed a fellowship in Female Pelvic Medicine and Reconstructive Surgery at The University of Alabama at Birmingham, under the supervision of internationally recognized Urogynecologists Dr. Ed Varner and Dr. Holly Richter. The fellowship was three years in length and accredited both by the American Board of Urology and the American Board of Obstetrics and Gynecology.

After completing my fellowship, I accepted a position as Assistant Professor of Obstetrics & Gynecology at The University of Tennessee Medical Center in Knoxville, TN, where I established the Division of Urogynecology.

I am Board Certified in both Obstetrics & Gynecology and Female Pelvic Medicine & Reconstructive Surgery. I am a Fellow of the American College of Obstetricians and Gynecologists, a Fellow of the American College of Surgeons, and a Diplomate of the American Board of Obstetrics & Gynecology.

I am a member of several societies who strive to improve the overall health and quality of life in women, including the American Urogynecologic Society (AUGS), Society of Gynecologic Surgeons (SGS), and the International Continence Society (ICS). I have published numerous journal articles, as well as book chapters in the fields of Gynecology and Urogynecology, have presented my research findings at both national and international conferences on women's pelvic

health, and have travelled to African nations volunteering medical services to women with life-altering gynecologic issues without access to routine healthcare.

I currently serve as Director for the Division of Female Pelvic Medicine and Reconstructive Surgery at The University of Tennessee Medical Center in Knoxville, TN, where I practice 5 days per week, varying my time between in-office evaluation, non-surgical and surgical management of patients with pelvic floor defects, as well as education of medical students, residents, and other faculty physicians.

Throughout my career, I have performed thousands of pelvic floor reconstructive procedures to treat and cure pelvic organ prolapse, urinary incontinence, fecal incontinence and multiple other pelvic floor issues, and have extensive experience in dealing with complications that arise from each. I am proficient in correcting pelvic organ prolapse both with and without the use of mesh, including abdominal, laparoscopic and robotic sacral colpopexy, vaginal hysterectomy, intraperitoneal and retroperitoneal uterosacral vault suspension, sacrospinous ligament fixation, colporrhaphy and hysteropexy. I am also proficient in the use of mid-urethral slings for the treatment of stress and mixed urinary incontinence and continue to use those weekly in my management of patients seeking more definitive treatment options. I am also trained in the use of and commonly perform neuromodulation procedures for the treatment of urge urinary and fecal incontinence.

In addition to surgical management, my expertise extends to the daily use of diagnostic testing for urinary and fecal incontinence including simple and complex urodynamic assessments, in-office cystoscopy, anorectal manometry, and endoanal ultrasound. I devote a significant amount of my day seeing patients with both stress and urge incontinence, voiding dysfunction, urinary retention, recurrent urinary

tract infections, and surgical complications leading to fistulae.

I am considered one of the leading experts in the southeastern United States region for native tissue repairs, mesh augmented prolapse procedures, anti-incontinence procedures, as well as surgical revision of complications related to vaginal mesh implant procedures.

I have trained with and performed the Gynecare TVT procedures since 2004 and have successfully completed over 2000 retropubic sling procedures since that time. I have also performed hundreds of transobturator slings.

I trained with and performed the Gynecare Prolift procedure in excess of 500 times (Anterior, Posterior and Total) beginning in 2007 and continuing until their production was halted in 2012, and contend, to this day, that the Prolift system was the single best vaginal approach prolapse repair kit ever available.

I have extensive knowledge of pelvic floor anatomy and have taught pelvic floor anatomy courses via the use of cadavers to both residents and faculty members, both at The University of Alabama at Birmingham and The University of Tennessee Medical Center in Knoxville.

I incorporate my extensive knowledge of pelvic floor anatomy, diagnostic skills, surgical and non-surgical treatment of pelvic floor abnormalities, and, specifically, my knowledge of Ethicon's Prolift/Prolift+M & Gynemesh into this report. All of my opinions are held to a reasonable degree of medical and scientific certainty. I reserve the right to amend this report and my opinions pending receipt of additional materials.

II. Materials Reviewed

In preparing this expert report, I have performed an exhaustive study of the scientific literature including Cochrane reviews, randomized controlled trials (RCTs) and peer-reviewed research studies of the highest caliber, detailing decades of opinions and scientific findings in the treatment of pelvic organ prolapse including surgical and nonsurgical repairs, via both mesh augmented repairs and native tissue repairs. In addition to the medical literature cited at the end of this report and on my reliance list, I have also performed a review of Ethicon's surgeon resource monograph, professional education materials, the Gynemesh and Prolift instructions for use and other company documents. Additionally, with almost 15 years of experience utilizing and inserting Gynemesh materials in the treatment of prolapse and incontinence, I have chosen to incorporate years of personal experience in the diagnosis and treatment of pelvic organ prolapse as well as associated complications.

III. Fees

My hourly rate for review of materials and drafting this report is $600.00. Deposition fees are $4000.00 for up to 4 hours and $6000.00 exceeding 4 hours + any additional travel expenses. Fees for trial testimony are $7500.00 daily + any additional travel expenses.

IV. Expert Opinion

I hold the above opinions to a reasonable degree of medical and scientific certainty. All opinions have been compiled based on my education, training and

professional experience as a gynecologic surgeon. Additionally, I utilize my significant background in evaluating, diagnosing and treating women with pelvic floor pathologies, annual participation in national and international meetings on women's pelvic health, as well as an extensive review of the available medical literature as it pertains to prolapse treatment, including surgical and non-surgical strategies. I reserve my right to amend or supplement this opinion based on new information that becomes available.

A. Background of Pelvic Organ Prolapse

Pelvic organ prolapse is the descent of one or more of the female pelvic organs (i.e. bladder, colon, uterus/cervix, vagina or small bowel) into the vaginal canal and/or protrusion of those organs through the vaginal opening. It is typically caused by a combination of weakening pelvic floor musculature and defects in the support structure of the pelvic organs secondary to childbirth, but risks are increased with age, connective tissue abnormalities, and the performance of activities of daily living (lifting, exercise) or medical conditions that lead to increases in intra-abdominal pressure (chronic cough, chronic constipation).

Prolapse of the pelvic organs affects approximately 50% of women over the age of 50 and is a common indication for gynecologic surgery and is found on routine examination in up to 60% of parous women (Hendrix 2002, Handa 2004). Prolapse of the pelvic organs can have an enormous negative impact on a woman's well-being. The presence of prolapse, many times, stands in the woman's way of completing daily tasks, and also limits her ability to engage in enjoyable activities. It is also a major health burden for some, as many women detail an inability to

exercise secondary to pain and pressure, and thus end up gaining weight, which can further worsen their overall symptoms. Additionally, it affects their self-perception and sexuality, many times leading to anxiety, even depression. In a 2010 study, Chiara, et al sought to compare depressive symptoms in women with and without prolapse and to evaluate impact on quality of life before and after surgery for prolapse. They found women with pelvic organ prolapse had a higher prevalence of depressive symptoms compared to controls without prolapse. Chiara et al also demonstrated that depressive symptoms improved following reconstructive surgery, with over 2/3 of those cases involving mesh augmentation.

Wu's study from 2009 (Wu Obstet Gynecol 2009; 114:1278) placed the overall prevalence of symptomatic pelvic organ prolapse at over 3 million – 3 million women suffering from complaints of pelvic pain, pressure, defecatory and voiding dysfunction, and other quality of life issues including self-perception and sexuality. Wu's study also indicates that the prevalence is expected to increase dramatically over the next 30 years, with an estimate of nearly 5 million affected by 2050. Olsen (1997) provided the classically quoted 11% lifetime risk that a woman will undergo at least one operation for pelvic organ prolapse (herein after referred to as POP) or stress urinary incontinence (herein after referred to as SUI) in her lifetime.

POP also leads to other health issues that dramatically affect quality of life (herein after referred to as QoL). The mere presence of pelvic organ prolapse increases urinary incontinence, lower urinary tract symptoms, and even urinary retention, which can lead to pain and chronic infections. Ellerkmann's study in 2001 reported that among women with symptomatic POP, 87% reported frequency/urgency, 73% reported urinary incontinence and 50–60% reported symptoms of voiding dysfunction (Ellerkmann et al 2001). Voiding dysfunction,

and defecatory dysfunction related to pelvic organ prolapse may require a woman to reduce the prolapse with her fingers in order to urinate or have a bowel movement. Dysuria, dyschezia, pressure and pain can occur from obstructive urinary or defecatory voiding dysfunction.

Another detriment to women with pelvic organ prolapse is in the form of decreased sexual function and a lower sexual quality of life (QoL). Multiple studies have shown significant links between the presence of pelvic organ prolapse, altered body image and sexual dysfunction (Lowenstein 2009, Athanasiou 2012, Lukacz 2016). In fact, the mere presence of prolapse is enough to interrupt sexual QoL, as studies have shown that the actual degree of prolapse holds no bearing on satisfaction; it's simply the presence of any symptomatic POP that alters self-perception and negatively affects sexual function (Athanasiou 2012). Multiple RCTs (described below) also show improved sexual function following repairs with mesh augmentation, with improving dyspareunia complaints following correction.

Many times, women can no longer tolerate their symptoms and seek assistance from gynecologic surgeons, Treatment strategies for symptomatic POP are wide ranging, from simple monitoring, pelvic floor exercises (Kegels) and pessaries to vaginal approach, laparoscopic/robotic approach, and open approach surgical repairs with and without the use of mesh augmentation. The decision for the desired treatment is usually made based on the degree of severity each patient experiences. Smaller stage (Stage I or early Stage II) prolapse may require no treatment at all, while others may choose to utilize exercises or pessaries to reduce the prolapse and feel more confident about their self-image. Later stage prolapses (Stage II beyond the hymenal ring or Stage III/IV) open the door to surgical

repairs. While pessaries can be used for some of these prolapses, issues of enlarged genital hiatus, or patient discomfort may preclude their use. Surgery to resuspend the vaginal apex (paramount in reducing overall recurrence risks) can be accomplished via native tissue repairs (uterosacral and sacrospinous fixations) or mesh augmented repairs (transvaginal approach or sacral colpopexy).

B. Non-Surgical Options

While pessaries have been shown safe and effective in multiple clinical trials, the bother and side effects of pessary use cause many women suffering from pelvic organ prolapse to discontinue their use and opt for surgical treatment. Symptoms of vaginal discharge, odor, bleeding and even erosion of the surrounding vaginal tissue can be bothersome to those looking for relief of their prolapse. When these symptoms occur, pessaries often times must be removed for a certain period of time to allow healing, thus switching the patient's symptoms back to pain, pressure and protrusion from their prolapse. A study by Sarma (BJOG 2009) showed that 56% of women utilizing pessaries for symptomatic prolapse experienced complications comprising bleeding, extrusion, severe vaginal discharge, pain and constipation. Only 14% continued with pessary use over the 6-year study period.

Additionally, some women are self-conscious about the use of a pessary. We attempt, in my practice, to utilize pessaries as a first-line therapy for symptomatic prolapse. We find, many times however, that women, particularly those that are still sexually active, are opposed to the idea of a pessary and the long-term management that goes along with their use.

Difficulty with self-removal and insertion of pessaries also limit their widespread use. Older, non-sexually active women with pelvic organ prolapse, sometimes lack the dexterity required to remove and insert their pessaries, requiring multiple trips per year to their physician for management. Women in this older age group also routinely exhibit vaginal atrophy unless they are on maintenance estrogen therapy. Therefore, women in this age group must not only manage their pessary, but also must keep the surrounding vaginal tissue healthy with applications of localized estrogens multiple times per week.

While pessaries can serve as a first-line therapy for some with symptomatic prolapse, they carry complications and obstacles many women are not willing to endure.

C. Non-Mesh Surgical Options

While non-mesh treatments for pelvic organ prolapse have been available for decades, so have the relatively high failure rates and the overall complications that go along with native tissue repairs. Issues with vaginal scarring, vaginal pain, exposure of suture materials, dyspareunia and lifetime recurrences exceeding 30% in multiple trials limit the native tissue repair's ability to provide long-lasting and complication-free outcomes.

Additional problems with native tissue repairs revolve around the overall lack of strength of the pelvic floor in those with prolapse. Multiple studies (Ulmsten 1987, Gilpin 1989, Norton 1992, Cosson 2003) have demonstrated weakening in the collagen matrix of women with pelvic organ prolapse. This is likely the primary

reason native tissue repairs fail and where augmentation with mesh can be beneficial.

Native tissue repairs work by intentionally causing vaginal scarring. Since there is no way to restore the strength of the pelvic floor connective tissue, procedures like colporrhaphies must rely on sutures to scar one area of tissue to another in an attempt to repair the defect. As a full-time practicing Urogynecologist, I can attest to the fact that some of the worst cases of vaginal scarring I have seen in patients referred to me for management involve those that had overly aggressive native tissue repairs utilizing only sutures.

Suture exposure is also common in native tissue repairs. Apical suspension, paramount in decreasing overall recurrence risks, are often times performed using permanent or delayed absorbable sutures. Some of Plaintiff's Experts actually describe their own technique of utilizing permanent sutures in vault suspensions, while neglecting to concede that the use of permanent suture in the vagina can lead to scarring, pain and exposures requiring reoperation. Studies looking at the rates of exposure of suture used in native tissue repairs showed a high rate of suture related complications and high failure rates. Toglia and Fagan reviewed the post-operative findings in 64 patients undergoing sacrospinous ligament fixation native tissue repair for symptomatic pelvic organ prolapse in a retrospective cohort study. They found an overall suture complication rate of 36%, which included exposure, granulation tissue and vaginal bleeding. They also showed a recurrent prolapse rate of 27% over an average follow-up of just over 2 years. (Toglia 2007)

Similar studies (Yazdany 2010) looked at patients undergoing a different type of native tissue apical suspensions via the uterosacral ligament. That retrospective

cohort analyzed 83 patients over 5 years treated for symptomatic pelvic organ prolapse with a traditional uterosacral suspension utilizing No. 0 permanent polyester suture (Ticron). Thirty-seven patients (44.6%) had suture related complications within 2 months of placement. Thirty of the 83 (36.1%) experienced suture exposure, with documented complications of granulation tissue, vaginal bleeding and vaginal discharge with half of those requiring additional treatments of silver nitrate application or removal of sutures. That cohort demonstrated nearly a 15% prolapse recurrence rate over the mean follow-up time of only 10.4 months.

Dyspareunia, or painful intercourse, is a known complication from any vaginal surgery – whether mesh augmented or native tissue in origin. A randomized controlled trial (herein after referred to as RCT) by Nguyen, et al comparing mesh augmented vs native tissue repairs in the anterior compartment (Obstet Gynecol 2008 Apr;111(4):891-8) showed the rate of de novo dyspareunia (painful intercourse following POP repair) was actually higher in the native tissue colporrhaphy group (16%) vs the mesh group (9%). That same RCT, looking at recurrence rates and complications showed significantly higher failure rates in the native tissue arm, noting that "nine anterior colporrhaphy patients would have to have recurrent anterior vaginal prolapse to prevent one vaginal mesh extrusion." Studies like Dr. Nguyen's clearly show the risk/benefit profile of mesh augmented repairs.

There remain other serious complications that are known risks of native tissue repairs. Ureteral injuries have been noted in up to 11% of native tissue repair uterosacral suspensions (Barber Am J Obstet Gynecol. 2000), while persistent buttock pain of 4.3% and other serious complications of rectal injuries and

neurovascular injuries have been shown in numerous studies evaluating sacrospinous ligament fixations.

There is an abundance of surgical outcome and satisfaction data comparing native tissue repairs to mesh augmented repairs and a sampling of those will be covered in the section on systematic reviews and recurrences.

D. Mesh Augmented Surgical Options

The goal of surgical correction of pelvic organ prolapse is to restore anatomic function, anatomy and support. While a number of surgical routes and procedures are available in the armamentarium of the gynecologic surgeon, the ideal surgery should lead to long-term successful outcomes with minimal risk of recurrence and complication. While no surgery is without a risk of both, surgeons became frustrated with the high failure rates patients were experiencing without augmentation strategies available, with failure rates quoted between 30% (Olsen 1997) and 58% (Clark 2003, Whiteside 2004). Marchionni et al showed 60% of recurrences occurred at the same site of repair (J Reproduct Med 1999) while Clark et al showed that one-third of recurrences occur in a different compartment as a result of "unmasking" of occult support defects (Am J Obstet and Gynecol 2003). The basis for the use of mesh in gynecologic surgery was the same as it was for the use of mesh in hernia repairs dating back to the 1950s – to augment the overall strength of the repair thus leading to a lower risk of recurrence. As stated above, multiple studies have demonstrated the weakening in the collagen matrix of women with pelvic organ prolapse. Augmentation with mesh can be beneficial in many women as detailed below.

Polypropylene, despite assurances from plaintiff's counsel, has been shown safe and effective for decades. Prolene polypropylene suture, the entity comprising the matrix of Gynecare/Prolift grafts was deemed "safe and effective for use" by the FDA in 1969 (B.H. Minchew, MD, Director of the FDA's Bureau of Medicine). Since that time, polypropylene has been used extensively in not just urologic and gynecologic surgeries but surgeries throughout the entire body. Multiple other clinical trials have demonstrated the overall safety of type I polypropylene (Rezapour 2001, Ulmsten 2001, Nilsson 2001).

Synthetic meshes were studied in abdominal approach outcome trials in the mid 1990s, with Benson, et al. showing better surgical outcomes in mesh augmented repairs when compared to native tissue repairs. Benson's study, comparing native tissue sacrospinous fixation to abdominal sacral colpopexy utilizing mesh showed a greater than two-fold reoperation rate in the native tissue repair arm. While the use of mesh in treating stress urinary incontinence was already quite common in the early 1990s, the commonplace utilization of mesh for prolapse repairs began in the later 1990s after studies like Benson's showed evidence of improved outcomes. Later, a Cochrane review confirmed Benson's findings showing mesh-augmented sacral colpopexy gave superior functional and anatomic results when compared to native tissue repairs. The same review also showed lower rates of post-operative dyspareunia in the mesh-augmented group compared to the native tissue group (Maher 2008). As Benson was demonstrating increased outcomes in abdominal approach mesh augmented repairs, Julian was performing the first randomized controlled trial on transvaginal mesh compared to native tissue repairs. Julian randomized women who had recurrent cystoceles to either a traditional colporrhaphy (native tissue repair) or an augmented repair utilizing permanent

transvaginal mesh. After following the patients for 2 years, he found a recurrence rate of 0% in the transvaginal mesh group compared to a 33% recurrence in the native tissue group. Three patients in the mesh augmented group experienced complications from the mesh (exposure/granulation tissue) (Julian 1996).

Gynemesh PS

In the early 2000's, prior to the development of Prolift, Gynemesh, a sheet of monofilament, macroporous, polypropylene mesh, with high biocompatibility, was heavily utilized as a way to augment prolapse repairs. Surgeons were utilizing sheets of Gynemesh and cutting them to perform both sacral colpopexies as well as vaginal approach repairs. This was done, following Benson's and Julian's data, in an effort to improve overall outcomes and decrease the recurrence rates. As surgeons were cutting Gynemesh to augment repairs, certain surgeons were also documenting various techniques of using Gynemesh sheets cut to specific shapes and sizes, detailing their own experiences with insertions. There was, however, no standardized shape or insertion technique. The French Transvaginal Mesh Group set out to change this, looking for a way to standardize the augmentation of pelvic organ prolapse repairs in an effort to build on early evidence showing improved outcomes with the utilization of mesh in POP repairs. The standardization of repairs, in addition to improving overall patient outcomes, lends itself to the ability to more easily and cost-effectively produce high-quality scientific studies, detailing outcomes with high-quality data.

Based on the biocompatibility and overall design of Gynemesh, the French Transvaginal Mesh (TVM) Group selected Gynemesh PS/Prolene Soft Mesh for its study on the graft that would eventually become Prolift. Utilizing that very graft,

they studied the concept of Prolift in over 600 women with pelvic organ prolapse. Those individuals were followed at one, three and five years and evaluated. This provided significant, meaningful, pre-market testing of the Prolift device and met with all industry standards for mesh used to treat prolapse. The cut of the mesh utilized in the studies of the French TVM Group was virtually identical to the end product cut and design of Prolift. Additionally, the insertion tools (or trocars) were almost identical to those later used in the Prolift kit. This would be the progression that surgeons would expect – high participant, high-quality studies with an implantable product that would see only slight variations of the mesh and tools available to patients compared to the implantable mesh and insertion devices that were studied extensively.

Members of the French TVM Group revealed follow-up Prolift study results in 2007 (Fatton Int Urogynecol J Pelvic Floor Dysfunct. 2007) which showed a mesh exposure rate of less than 5% with only 2 patients requiring surgical management, and a surgical failure/recurrence rate of 4.7%. This study involved anterior, posterior and total Prolift products.

As Prolift was developed, surgeons were able to offer some of the advantages of transvaginal mesh to their patients, namely decreasing recurrence rates, particularly in the anterior compartment where the vast majority of recurrences are seen. Prolift was studied more than any other transvaginal mesh kit in history with over 100 studies documented in the medical literature, and became the preferred choice for treating large, symptomatic and/or recurrent prolapses.

E. Systematic Reviews / Recurrences / Comparative Complications

Recurrences

For years, the debate has centered around short-term and long-term success rates of native tissue repairs vs mesh-augmented procedures. Cochrane Reviews measure benefits and harms by collecting data from more than one trial and combining them to generate an average result. This aims to provide a more precise estimate of the effects of an intervention and accomplishes this while reducing uncertainty. Cochrane meta-analyses offer a comprehensive review of randomized controlled trials (RCTs). They offer the highest level of clinical evidence (Level I) and are considered to be the most reliable source of evidence to guide clinical practice.

In addition to multiple studies including RCTs, we will include Cochrane reviews in this discussion on recurrences. In doing so, I hope to paint a picture of what today's landscape is regarding native tissue vs mesh-augmentation compared to what the landscape was during the use of Prolift.

Cochrane Reviews/Systematic Reviews

Maher et al published a 2013 Cochrane review analyzing 56 RCTs comprising almost 6000 women. Here are some key Maher findings regarding mesh augmented vaginal approach prolapse repairs:

-Standard anterior repair (native tissue) was associated with more anterior compartment prolapse on examination than for any polypropylene (permanent) mesh repair.

-Awareness of prolapse was also higher after the anterior repair (native tissue) as compared to polypropylene mesh repairs.

-The use of grafts (biological or synthetic) reduces the risk of prolapse symptoms and recurrent anterior vaginal prolapse on examination when compared to native tissue repairs (colporrhaphy). However, the advantages of a permanent polypropylene mesh must be weighed against disadvantages including longer operating time, greater blood loss, prolapse in other areas of the vagina, new onset urinary stress incontinence, and the mesh becoming exposed in the vagina in 11% of women.

-In general, there is a lack of evidence to support transvaginal mesh operations used in apical or posterior compartment surgery.

These 56 RCTs were comprised of many types of transvaginal mesh – not Prolift alone.

Maher et al also published a 2016 Cochrane review analyzing 37 RCTs comprising over 4000 women. Here are some key Maher findings regarding mesh augmented vaginal approach prolapse repairs:

-Evidence suggests that if 15.5% of women had awareness of prolapse after mesh repair, then 5.6% to 30.9% would have awareness of prolapse after native tissue repair.

- There is no conclusive evidence that POP surgery with mesh increases repeat surgery for SUI.

-There is little or no difference between the groups (mesh vs native tissue) in rates of de novo SUI or dyspareunia.

-Awareness of prolapse at one to three years was less likely after mesh repair.

-Rates of repeat surgery for prolapse were lower in the mesh group. This suggests that if 38% of women have prolapse on examination after native tissue repair, between 11% and 20% will have prolapse on examination after transvaginal mesh repair. More women in the mesh group required repeat surgery for the *combined outcome* of prolapse, stress incontinence, or mesh exposure.

-Recurrent prolapse on examination was less likely after mesh repair.

-Permanent mesh was associated with higher rates of de novo stress incontinence; however, there was no evidence of a difference between the groups in the rate of repeat surgery for stress urinary incontinence.

-There was no evidence of a difference between the groups in rates of de novo dyspareunia.

-Effects on quality of life were uncertain.

These 37 RCTs were comprised of many types of transvaginal mesh – not Prolift alone.

Schimpf et al published a 2016 Systematic Review analyzing 66 comparative studies reported in 70 articles, including 38 RCTs. Here are some key Schimpf findings regarding mesh augmented vaginal approach prolapse repairs:

-Posterior compartment: no difference in anatomic and quality-of-life outcomes when using synthetic absorbable mesh, synthetic nonabsorbable mesh, or biologic graft compared with native tissue for transvaginal repair of posterior vaginal prolapse. Graft exposure and complication rates were low.

-Anterior compartment: the use of mesh consistently resulted in improved anatomic outcomes compared with native tissue repair. A large study in this review, by Altman et al, randomized 389 women to either a Prolift mesh kit or native tissue anterior colporrhaphy, showing that mesh improved anatomical outcomes, but pain and sexual function were not statistically different between groups. Regarding bulge symptoms and Pelvic Organ Prolapse-Distress Inventory scores, both meta-analyses significantly favored the use of mesh, finding that it improved prolapse symptoms as measured by Pelvic Organ Prolapse-Distress Inventory and based on numbers of women with bulge symptoms.

-In summary, there is high-quality evidence that the use of synthetic nonabsorbable mesh improves anatomic outcomes compared with native tissue anterior colporrhaphy. Data from meta-analyses confirm that mesh repairs also provided superior relief of subjective bulge symptoms. However, there is also high-quality evidence to suggest no difference for subjective outcomes including quality of life and urinary and sexual function.

-Across studies, erosion rates generally ranged from 1.4–19%, with most of these treated in the office. Operative mesh revision rates ranged from 3–8% across

studies. *When reported, there were rarely significant differences between groups for overall reoperation rates.*

-Prolapse anatomic outcomes favor mesh placement in most studies when the outcome of interest is overall POP-Q staging. When analyzed separately by vaginal compartment, results at the posterior and apical vaginal compartments showed no significant difference between arms, but the anterior vaginal compartment outcomes always favor mesh use for a better anatomic result.

-Post-operative dyspareunia and urinary incontinence rates do not significantly differ between arms in any study

Other RCTs

As stated above, analysis of these RCTs in these Cochrane reviews was comprised of many types of transvaginal mesh – not Prolift alone. There were however, several randomized controlled trials (RCTs) prior to the Cochrane reviews that concentrated on Prolift alone.

Altman et al looked specifically at the Gynecare Anterior Prolift system and randomized 389 women to study treatment – 200 had prolapse repair utilizing Prolift; 189 underwent traditional native tissue colporrhaphy. The primary outcome was a composite of the objective anatomical designation of stage 0 (no prolapse) or stage 1 (position of the anterior vaginal wall more than 1 cm above the hymen), according to the Pelvic Organ Prolapse Quantification (herein after referred to as POP-Q) system, and the subjective absence of symptoms of vaginal bulging 12 months after the surgery. At 1 year, the primary outcome (stage 0 or stage 1

prolapse) was significantly more common in the women treated with transvaginal mesh repair (60.8%) than in those who underwent colporrhaphy (34.5%), i.e. the failure rate of the procedure to obtain Stage 0 or 1 support after 1 year was 39.2% in the Prolift arm and 65.5% in the native tissue arm. While blood loss and operative times were increased in the mesh group, only 6 patients required reoperation for a mesh related complication. No differences were noted in pain, dyspareunia, or sexual function between the two groups post-operatively.

Withagen et al also studied Prolift specific mesh augmented procedures, comparing Prolift in multiple compartments to native tissue repairs alone in a Level I RCT of almost 200 women. All procedures were conducted by gynecologic surgeons with broad experience in pelvic floor reconstruction. Native tissue repairs consisted of one or a combination of the following: traditional anterior colporrhaphy, posterior colporrhaphy, uterosacral suspension, or sacrospinous fixation – depending on the given defect of each study participant. The primary endpoint was anatomic failure (Stage II prolapse or higher) in any compartment at 12 months post-operative. Secondary endpoints observed potential complications for each group including blood loss, length of [hospital] stay (LOS), pain, dyspareunia, and SUI. At 12 months post-surgery, anatomic failure was observed in 45.2% of those treated with native tissue repair, while only 9.6% of mesh augmented women experienced failure. Operating time was higher in the mesh group, however, only by 8 minutes. There was no difference in LOS, nor blood loss, although one patient in the native tissue group required reoperation secondary to post-operative hemorrhage. There was no difference in post-operative dyspareunia rates, with both groups experiencing a decrease in pain with intercourse after intervention. There was no difference in de novo SUI or pain. Cumulative mesh exposures were at 16.9% in the mesh group – a total of 14 patients over one year. Of these 14 patients, 9 were

asymptomatic and treated with estrogen. Five underwent a simple day surgery procedure for excision and reclosure with total resolution.

A 2012 RCT by Halaska et al evaluated women undergoing surgery for Stage II or greater vault prolapse, comparing the use of a total Prolift vs native tissue sacrospinous ligament suspension +/- anterior and posterior colporrhaphy. At 12 months, 72 women were evaluated from the native tissue group, 79 from the mesh group. Prolapse recurrence was seen in 16.9% of the mesh participants, while 39.4% of the native tissue participants suffered a prolapse recurrence, with the anterior compartment having the highest rate of recurrence. A total of 16 patients in the mesh group (20%) experienced a mesh exposure. Ten of these were treated with simple resection, while 6 resolved with topical estrogen therapy. There were no statistical differences in operative blood loss, or post-operative issues of UTIs, de novo SUI, de novo overactive bladder (OAB), pelvic pain or dyspareunia between the groups. No significant differences were observed in quality of sexual life between the native tissue sacrospinous ligament suspension and mesh groups as measured by the Prolapse Impact Sexual Questionnaire (PISQ) short form. The authors found a significant improvement in all the domains of the Urinary Impact Questionnaire (UIQ), Colorectoanal Impact Questionnaire (CRAIQ), and the Pelvic Organ Prolapse Impact Questionnaire (POPIQ) after the surgery within both groups, but no significant differences were observed between the sacrospinous ligament suspension and mesh groups. There was, however, less improvement of bowel symptoms (CRAIQ) in the native tissue group compared to the mesh group.

A similar single-center, randomized controlled trial by Svabik in 2014 compared the use of a total Prolift vs. native tissue sacrospinous ligament suspension +/- anterior and posterior colporrhaphy. After randomization of 70 women with post-hysterectomy vault prolapse (36 Prolift, 34 native tissue), patients were evaluated

at 1-year post-operative for possible anatomic failures – defined as recurrent prolapse to the level of the hymenal ring or beyond. Results from Svabik's study were striking, with only 1 (3%) anatomical failure in the Prolift group after one year, and 22 (65%) failures in the sacrospinous native tissue group. While more women developed de novo SUI following Prolift, that finding correlated with the higher prolapse recurrence rate in the native tissue group which likely increased the incidence of urethral kinking decreasing de novo incontinence rates in the non-mesh group. Three women in the mesh group experienced mesh exposures within the first 12 months. Five women experienced vaginal bleeding and granulation tissue – all of those were in the native tissue group.

da Silveira's 2014 multicenter randomized trials included 184 women with POP-Q Stage III or IV prolapse. Patients were randomized to either treatment with native tissue sacrospinous ligament fixation +/- anterior and posterior repair or Prolift mesh augmented repairs. Hysterectomy was performed at the time of either intervention as needed for uterine prolapse. At one-year post-operative, anatomic cure rates were noted to be significantly better in the anterior mesh augmented group. Of note, in this RCT, greater improvements were seen in Prolapse Quality of Life Questionnaire (PQoL) scores in the mesh-augmented group. No differences were seen between the groups with regard to operative time, complications or post-operative pain. Dyspareunia was actually higher in the native tissue group, though not statistically significant. Also of note, while 18 patients did experience mesh exposure, 6 in the native tissue group experienced suture exposure requiring outpatient treatment.

Other studies have not only confirmed the high failure rates of native tissue repairs but have also pointed out significant suture exposure complications. Estimates for recurrent anterior vaginal wall prolapse after sacrospinous ligament fixation

(herein after referred to as SSLF) have been as high as 40%. (Sze EH, Karram MM. Transvaginal repair of vault prolapse. Obstet Gynecol. 1997;89(3):466-475; Morgan DM, RogersMA, Huebner M,Wei JT, Delancey JO. Heterogeneity in anatomic outcome of sacrospinous ligament fixation for prolapse. Obstet Gynecol. 2007;109(6):1424-1433.). Additionally, the OPTIMAL RCT, a multi-center, randomized controlled trial of 374 women undergoing repair of apical vaginal prolapse compared SSLF and uterosacral vault suspension (herein after referred to as USVS). While the unusually high rates of recurrent prolapse seen post-operatively were partially due to stringent outcome measures, nearly 20% of the participants developed bothersome vaginal bulge symptoms by 2 years. The most common long-term complications among the 374 women was granulation tissue (16.6%) and exposure of implanted suture (16.3%). (Barber, 2014)

Complications

While Plaintiff's experts are quick to point out studies with high exposure rates, they neglect to show other studies that show exposure rates of suture material used in native tissue repairs to be as high, and in some cases higher than those seen in mesh augmented repairs. Many times, as shown in these studies, additional surgical management is required to resect permanent sutures, and, as we've seen countless times, revision of scar bands, sinus tracts and chronic granulation tissue are not uncommon.

Studies looking at the rates of exposure of suture used in native tissue repairs showed a high rate of suture related complications and high failure rates. As previously described, Toglia and Fagan reviewed the post-operative findings in 64

patients undergoing native tissue sacrospinous ligament fixation native tissue repair for symptomatic pelvic organ prolapse in a retrospective cohort study. They found an overall suture complication rate of 36% which included exposure, granulation tissue and vaginal bleeding. (Toglia 2007) Also, as previously described, Yazdany looked at patients undergoing native tissue apical uterosacral suspensions in a retrospective cohort analyzing 83 patients over 5 years treated for symptomatic pelvic organ. Thirty-seven patients (44.6%) had suture related complications within 2 months of placement. Thirty of the 37 (36.1%) experienced suture exposure, with complications of granulation tissue, vaginal bleeding and vaginal discharge, with half of those requiring treatment/removal of granulation tissue or removal of sutures. Of note, that native tissue cohort demonstrated a nearly 15% prolapse recurrence rate within the mean follow-up time of only 10.4 months.

Long Term Studies

Many of the RCTs and reviews listed above, and most of the data we have comparing mesh to native tissue repairs is of short-term data. Looking at long-term data of the Prolift system, we see continuing benefit in objective and subjective outcomes, continuing benefit in quality of life symptoms and low complication rates. A long-term objective and subjective retrospective analysis performed at my alma mater looked at women who underwent prolapse surgery utilizing Prolift mesh augmentation for symptomatic POP. In the study (Meyer, 2015), the mean duration of follow-up was 7 years. POP-Q measurements of Ba, Bp, C, GH and PB were all significantly improved following Prolift augmentation. Overall POP-Q stage was significantly improved following Prolift augmentation.

And, validated questionnaires measuring quality of life in this population (Urinary Impact Questionnaire, POP Impact Questionnaire, Urinary Distress Inventory, and POP Distress Inventory) all showed significantly improved scores from pre-operative baseline. Subjectively, 80% of women in the study reported a complete absence of vaginal bulge symptoms at greater than 5-year follow-up, and nearly 85% reported satisfaction with their procedure. Mesh exposure was low at around 6% - a total of 3 patients – all of which had discontinued use of their estrogen cream and demonstrated significant vaginal atrophy on examination.

Heinonen et al (2016) also looked at long-term outcomes following Prolift augmented prolapse repairs. Median follow-up was again 7 years, and similar to the Meyer study, over 80% of patients voiced satisfaction with the procedure. Differing greatly, however, was the mesh exposure rate, with 23% experiencing an exposure – further evidence that surgical technique and insertion skill level (not the product itself) define the rate of complication, as further discussed below.

Stable anatomic repairs have been demonstrated in multiple other long-term studies on Prolift (Miller 2011, Kozal 2011, Khan 2014 to name only a few). Khan's study demonstrated anatomic cure rates after Prolift of almost 90% with only six patients (5.6%) experiencing a mesh exposure. Re-operation rate for a same compartment recurrence after Prolift was less than 3%.

In all of the above listed trials and RCTs, I have concentrated mainly of success and failure rates, as well as associated complications. Some of the surgical failures required re-operation; some did not. Some of the complications associated with repairs required re-operation; some did not. While Plaintiff's counsel will be quick to point out that the overall re-operation rate in the mesh group is higher, we should pay attention to what is occurring in these re-operation procedures. I am

considered one of the leading experts in mesh complications and removals in the southeastern US region, and I can state, without hesitation, that the vast majority of re-operations for mesh complications are extremely simple procedures, many times taking less than 15-20 minutes to complete, and can be done under monitored anesthesia care or local anesthesia. Therein lies the main difference in the re-operations. Re-operations for mesh complications are typically a simple excisional procedure (many times in the office) while re-operations for surgical failures secondary to weaker integrity native tissue repairs involve more in-depth procedures, such as abdominal, laparoscopic and robotic sacral colpopexies, and mesh augmented prolapse repairs. Some studies (Withagen 2011, Halaska 2012) even detail correcting patients' native tissue surgical failures with Prolift secondary to patient complaints of symptomatic recurrence. Operative procedure for mesh revisions (from exposures that cannot be handled by the simple application of estrogen vaginal cream) range across multiple clinical studies from 3-8%, based on Cochrane data. The operative time and the overall burden to the patient for a 15-minute mesh excision is far less than a major reconstructive procedure secondary to a recurrence of symptomatic prolapse.

Prolift+M

Prolift+M was developed in an effort to attempt to decrease the overall foreign material implanted – the thought being that less material would improve clinical outcomes.

Plaintiff's experts utilize certain Prolift+M studies in an attempt to show its failures, but in doing so, they demonstrate the graft's similar efficacy to Prolift. Additionally, their quoted studies show not only high success rates, but statistically significant improvement in sexual function and a re-operation rate for mesh exposure less than 6% (Milani 2011). Khandwala (2011) also demonstrated efficacy and safety of Prolift+M with erosions at less than 4%. While this trial did show improvements in both function and anatomy post-operatively, the trial did not compare Prolift+M to the traditional Prolift mesh. Cosson (2011) and Quemener (2014) similarly showed excellent functional improvements and improved anatomic support without apparent safety concerns.

Plaintiff experts have stated that a lighter weight mesh would have been preferable to the Gynemesh PS utilized in Prolift; however, there is no evidence to support their claim. Although the initial thinking behind the design of Prolift+M was that its lower density and decreased mesh load with improve outcomes, the data did not support the theory. Milani et al found in 2010 that although Prolift+M offered good anatomic support and no apparent safety concerns were noted, its clinical success was consistent with the original Prolift mesh. Other studies (Bhatia 2010) showed that while there appeared to be an improvement in post-operative sexual function of lower weight meshes compared to the standard weight Prolift, the benefit was only short-term. Lensen (2013) also showed that while mesh exposures were somewhat lower in the lower weight mesh, Prolift+M demonstrated similar subjective and objective cures when compared to the higher weight mesh in Prolift.

While there was no apparent benefit of the Prolift+M graft with regard to objective and subjective cure rates, the graft showed great promise and longer term studies were needed to confirm its long term success compared to standard Prolift. While

Prolift+M exhibited significant anatomic and functional outcomes, Plaintiff's experts have attempted to skew the data to show decreased success rates of the graft by counting patients who were lost to follow-up during the trials as "surgical failures" – a sloppy and unacceptable manipulation of the data.

F. Plaintiff's Expert Witness Opinions

Many of the same studies used by Plaintiff's experts trying to show the dangers of mesh-augmented repairs actually demonstrate the low risks of complications. Additionally, I have shown above, the large variance in mesh complication rates between different surgical centers despite the use of identical products, thus demonstrating that overall surgical skill plays an enormous role in not only surgical outcomes, but surgical complications. This may not be a popular topic, but it is unfortunately true and explains the variability one reads about in the medical literature concerning exposure rates. Several studies have shown extraordinarily low rates of mesh exposure. Benbouzid et al (2012) showed an 85% success rate with no recurrences at nearly 5 years following mesh-augmented prolapse repair. Over the length of the study, a mesh complication rate of around 5% was recorded. Meyer et al (described above) demonstrated a 6% exposure rate at 2 years and all had significant vaginal atrophy. In that study, all patients, at mean follow up of 7 years, had Stage II prolapse or less with 94% confined behind the hymenal ring. Kozal, 2014 demonstrated a low mesh augmented recurrence at 8%, surgical management for mesh exposure was low at 4.5%. This is a sample of many cases looking at mesh augmented repairs that show extraordinary long-term success rates with minimal complications.

Some Plaintiff's experts claim Prolift causes "life-altering and sometimes permanent injury and disability without proven benefit." The evidence shows otherwise. Any vaginal reconstructive procedure, as detailed above, mesh-augmented or native tissue in origin, can cause injuries. Exposures of sutures utilized in native tissue repairs are common, as detailed in many studies, and re-operations for not only the complications from native tissue repairs, but the proven increased risk of recurrence are common.

Some Plaintiff's experts claim "there is no good evidence supporting improved benefit in quality of life (QOL) or relief of symptoms in any compartment with the use of transvaginal mesh for the treatment of pelvic organ prolapse." This is blatantly incorrect. The randomized controlled trial by da Silveira, et al, described above, demonstrated QoL changes greater in the mesh group compared to the native tissue arm, and Halaska's RCT showed a higher improvement of bowel symptom quality of life on the CRAIQ in the mesh group over the native tissue arm. Meyer et al also used validated questionnaires measuring quality of life in a population of women 7 years post-operative from Prolift augmentation for symptomatic prolapse. Urinary Impact Questionnaire, POP Impact Questionnaire, Urinary Distress Inventory, and POP Distress Inventory all showed significantly improved quality of life scores from pre-operative baseline.

Some Plaintiff's experts claim "there is no reduction in reoperation rates for prolapse in any compartment with the use of transvaginal mesh for the treatment of pelvic organ prolapse." This is also an untrue statement. When comparing re-operation rates for prolapse alone in a Cochrane systematic review of over 4000 women, Maher (2016) demonstrated that "evidence suggests that there are

advantages to using transvaginal permanent mesh compared to native tissue repair, including lower rates of awareness of prolapse, reoperation for prolapse, and recurrent prolapse on examination."

Some Plaintiff's experts claim "there is no evidence of anatomic benefit with the use of transvaginal mesh for the treatment of pelvic organ prolapse in the posterior or apical compartments." While there is current evidence that mesh augmentation in the posterior compartment does not increase success rates compared to native tissue repairs alone, there is evidence to show differences in de novo alternate compartment failures when apical suspensions are compared to Prolift. As described above, Halaska's 2012 multi-center randomized, prospective, controlled trial comparing sacrospinous ligament fixation (SSLF) with mesh augmented prolapse repairs (Prolift), showed the prolapse recurrence rate was significantly higher at 12 months in the SSLF group (39.4%) than in the mesh group (16.9%). The most common location of recurrence in the SSLF group was the anterior compartment (16 of 28, 57.1 %).

Some Plaintiff's experts claim there is no evidence of anatomic benefit with the use of transvaginal mesh for the treatment of pelvic organ prolapse in the anterior compartment. This also is incorrect. Any recent study that showed no evidence of benefit does not override years of RCTs and Cochrane reviews with the highest level of scientific evidence which prove otherwise.

Some Plaintiff's experts claim that "many of these complications [associated with mesh augmented repairs] do not occur with traditional prolapse repairs." I would challenge Plaintiff's expert to produce a complication that occurs with the mesh utilized in Prolift/Gynemesh/Prolift+M that cannot also occur with the use of permanent sutures utilized in native tissue repairs. As already demonstrated by

Toglia's work, and as described in several case specific reviews I have completed thus far, the complication rates, and even the re-operation rates for suture related issues, can be quite high. Plaintiff's experts specifically point to "erosion, extrusion, perforation, partner injury, vaginal pain, pelvic pain, granulomas, bleeding, fistulae," and the need for additional surgical procedures to correct the complications. Every single one of these can occur with suture utilized in native tissue repair; in fact, I can personally attest to having corrected each one of these complications secondary to a suture utilized in a native tissue repair.

Some Plaintiff's experts claim that "these [mesh] complications can occur at any time – months or years after the original surgery, unlike complications occurring with traditional prolapse repairs." This is also an untrue statement. I have seen complications from native tissue repair and mesh augmented repairs present immediately after surgery, and I've seen others where the patients first complaints were years following the initial repair. There is no valid scientific evidence to back up Plaintiffs' expert's claim.

Some Plaintiffs' experts claim that "Many of these [mesh] complications are life-altering and permanent, unlike those seen with traditional prolapse repairs. There is no valid scientific evidence to back up this claim. I have personally corrected complications from native tissue repairs that caused horrible dyspareunia, pelvic pain, levator ani spasm, depression and a myriad of other complaints. Any vaginal surgery, mesh-augmented or native tissue in nature, can lead to life-altering, prolonged complaints. This is a basic tenet of vaginal surgery. The inherent risks of vaginal pain, vaginal scarring, dyspareunia, contraction, infection, recurrence and exposures of implantable material have been common knowledge among

gynecologic and urologic surgeons for decades. The implementation of the use of mesh to augment prolapse repairs and decrease recurrences did not change this.

The risks noted above - vaginal pain, vaginal scarring, dyspareunia, contraction, infection, recurrence and exposures of implantable material - are discussed on a near daily basis with medical students and OB/GYN residents on my Urogynecology rotation and elective at our academic medical center. Residents, even medical students, are taught from their first day on service, the inherent risks of any vaginal surgery. These same principles were taught to me as a medical student, reinforced ad nauseum as a medical resident, and further discussed during my fellowship. No surgeon performing gynecologic procedures of this magnitude can claim they are unaware that making any incision in the vaginal epithelium of a woman can lead to scarring, pain, dyspareunia, infection, recurrence or exposures. This is as basic as foley catheter management and should be expected knowledge of any gynecologic surgeon. In addition to everyday teaching of these basic tenets during training, a mountain of scientific literature has echoed the same, putting gynecologic surgeons on notice regarding complications possible in vaginal surgeries for literally decades prior to Prolift's official release (Dyspareunia Following Vaginal Surgery, Francis, 1961; Repair of post-hysterectomy vaginal-vault prolapse, Lane, 1962; Sexual life after gynaecological operations—II, Amias, 1975; The complications of colposuspension, Galloway, 1987; Influence of operations for Stress Incontinence and/or Genital Descensus on sexual life, Haase, 1988; Rectocele Repair; Four years' experience, Arnold, 1990; Pelvic Support Defects and visceral and sexual function in women treated with sacrospinous ligament suspension and pelvic reconstruction, Paraiso, 1996; Banked human fascia lata for the suburethral sling procedure: a preliminary report, Handa, 1996; Vaginal versus abdominal reconstructive surgery for the treatment of pelvic

support defects: a prospective randomized study with long-term outcome evaluation, Benson, 1996; Posterior colporrhaphy: its effects on bowel and sexual function, Khan, 1997; A new operation for genitourinary prolapse, Nicita, 1998; Should sacrospinous ligament fixation for the management of pelvic support defects be part of a residency program procedure? The University of Miami experience, Penalver, 1998; Failure of allograft suburethral slings, Fitzgerald, 1999; Complications of surgery of genuine stress incontinence, Chaliha, 1999; Erosion of fascial sling in to the urethra, Handa, 1999; Sexual function and vaginal anatomy in women before and after surgery for pelvic organ prolapse and urinary incontinence, Weber, 2000; Management of urethral erosion caused by a pubovaginal sling, Golomb, 2001; Pubovaginal sling using cadaveric fascia and bone anchors: disappointing early results, Carbone, 2001; Vaginal erosion of cadaveric fascia lata following abdominal sacrocolpopexy and suburethral sling urethropexy, Kammerer-Doak, 2002; Urethral erosion following autologous rectus fascial pubovaginal sling, Webster, 2003; TVT, TVT-O, Gynemesh, Prolift IFU; 2000 TVT Surgeon Monograph; Prolift Surgical Technique Guide; 2007 Prolift Surgeon Monograph; TVT, TVT-O, Gynemesh and Prolift Profession educational materials).

V. CONCLUSIONS

Prolapse of the pelvic organs can have an enormous negative impact on a woman's well-being. The presence of prolapse, many times, stands in the woman's way of

completing daily tasks, and also limits her ability to continue things she enjoys doing. It is also a major health burden for some, as many women detail an inability to exercise secondary to pain and pressure, and thus end up gaining weight, which can further worsen their overall symptoms.

While non-surgical treatments for pelvic organ prolapse have been available for decades, so have the relatively high failure rates and the overall complications that go along with native tissue repairs. Issues with vaginal scarring, vaginal pain, exposure of suture materials, dyspareunia and lifetime recurrences exceeding 30% limit the native tissue repair's ability to provide long-lasting and complication-free outcomes.

In the early 2000's, prior to the development of Prolift, Gynemesh, a sheet of monofilament, macroporous, polypropylene mesh, with high biocompatibility, was heavily utilized as a way to augment prolapse repairs. This was done in an effort to improve overall outcomes and decrease the recurrence rates. Gynemesh is still used today in abdominal, laparoscopic and robotic sacral colpopexies. I use Gynemesh frequently to this very day – with extraordinary success. Based on its biocompatibility and overall design, the Transvaginal Mesh Group selected Gynemesh for its study on the graft that would eventually become Prolift. Utilizing that very graft, they studied the concept of Prolift in over 600 women with pelvic organ prolapse. Those individuals were followed at one, three and five years and evaluated, showing great success as outlined above. This provided significant, meaningful, pre-market testing of the Prolift device and met with all industry standards for mesh used to treat prolapse.

After Prolift was developed, surgeons were able to offer some of the advantages of transvaginal mesh to their patients, namely decreasing recurrence rates, particularly in the anterior compartment where the vast majority of recurrences are seen. Prolift was studied more than any other transvaginal mesh kit in history, and became the preferred choice for treating large, symptomatic and/or recurrent prolapses.

The overall body of evidence for the use of mesh in gynecologic surgery is overwhelming. There were multiple studies that showed the graft's safety (Kozal 2014, Damoiseaux 2015, Meyer JMIG 2016, IUJ 2015, Heinonen, IUJ 2016) and multiple trials of randomized, controlled design that showed its superiority to native tissue repairs (Withagen 2011, Sokol 2012, Halaska 2012, Svabik 2014, Da Silveira 2014). The findings of superiority were noted in larger systematic reviews that are trusted as some of the highest level of scientific data today. Maher's 2016 Cochrane review showed that recurrent prolapse on examination was less likely after mesh repair. The same review showed that the rate of repeat surgery for prolapse was lower in the mesh-augmented group.

Additionally, Schimpf's 2016 review concluded "synthetic mesh augmentation of anterior wall prolapse repair improves anatomic outcomes and bulge symptoms compared with native tissue repair" and showed that even though mesh complications could occur, the risk of reoperation was low.

While exposures of mesh can certainly happen after insertion, so can those exposures of any implantable products – such as the permanent sutures used in native tissue repairs. Also, as stated above, many of the complications plaintiff's counsel tries to hang directly on the mesh, or the design thereof, the same occur with native tissue repairs. Issues with exposures of suture, vaginal scarring, vaginal

pain, and dyspareunia have been seen in vaginal surgery for decades - long before the introduction of mesh. And while plaintiff's counsel, through advertisements and scare tactics, would have the general public convinced of the mesh's "ability" to move around the body and wreak havoc, it's simply not the case. The vast majority of mesh exposures are small and asymptomatic. And those that do require treatment are typically easy to resolve in the right hands. As a full-time, practicing Urogynecologist, I remove symptomatic mesh and suture exposures as part of my practice. The overwhelming majority of patients experience a complete resolution of their symptoms following a quick revision procedure, and sometimes with simple application of vaginal estrogen creams. One must also keep in mind that revision procedures are also necessary, as outlined above, in the non-mesh augmented cases.

I have removed several pieces of mesh over my career. I can attest to the fact that complications from mesh procedures are many times related to the skill level of the surgeon. This may not be a popular topic, but it is unfortunately true and explains the variability one reads about in the medical literature concerning exposure rates. In all of the mesh that I have removed in my career, I have never once seen the alleged design defects that plaintiff's experts love to quote: "degradation," "cytotoxicity," "fraying," "particle loss," or "chronic inflammation." Other often-mentioned design defects of "roping," "curling" and "banding" are not related to the implant itself – but, rather related directly to improper placement of said product. In the treatment of POP and SUI, I have placed thousands of mesh implants over my career – as I'm certain Plaintiff's experts have done as well in the treatment of SUI. Based on my vast clinical experience and constant review the medical literature, I have seen no evidence that any of these alleged defects or characteristics of the mesh have any clinical significance - if they occur at all.

Claims that there is an ongoing chronic inflammatory reaction of clinical significance is also baseless. Any foreign object implanted in the body, whether mesh or suture used in native tissue repair, is expected to cause an inflammatory reaction. Active inflammatory reactions are acute and seen in the post-operative healing phase. There is no legitimate evidence to support the claim of an ongoing, active, and harmful inflammatory reaction in patients receiving mesh.

Any suggestions by Plaintiff's counsel regarding "mesh degradation" are also not supported by reasonable medical literature. We have solid, scientific evidence published in the International Urogynecology Journal that directly contradicts this claim. In Thames study, they found that "cleaning of explanted Prolene meshes and subsequent analyses showed that they did not degrade in vivo, confirming the in vivo stability of properly formulated polypropylene. Instead, the cracked layer that some researchers have identified as degraded Prolene is an adsorbed protein–formaldehyde coating, resulting from the well-established formalin–protein fixation process, which occurs immediately upon placing an explant in formalin." (Thames 2017)

Plaintiff experts contend that native tissue repairs (or other surgical procedures) would be a safer alternative design to Prolift / Prolift +M. These claims are baseless. There is no clinical evidence supporting plaintiff's counsel claims that a lighter weight, larger pore, partially absorbable mesh would be a safer alternative design. Clinical studies have shown similar efficacy, as well as similar complication rates between Prolift and Prolift +M, which is the exact light-weight, partially absorbable mesh plaintiff's counsel suggests. As a full-time pelvic reconstructive surgeon, I am not aware of any mesh that exists that is more

efficacious than Gynemesh, nor am I aware of any mesh available today that would eliminate or significantly reduce complications like exposure and dyspareunia that are inherent in any graft material, including permanent sutures commonly used in native tissue repairs.

The Prolift / +M's Instructions For Use (IFU) was not misleading as plaintiff's counsel suggests. The IFU adequately warned of potential complications. Ethicon provided professional education information which included potential complications. The Prolift Surgeon's Monograph, Prolift Surgical Technique Guide, as well as the IFU and professional education courses all warned of the risk of mesh exposure. The same monograph and same professional education warned of potential vaginal scarring, contraction, pain and dyspareunia - the same potential complications seen in native tissue repairs. Out of all of the chronic pelvic pain patients that are sent to me from an extremely large treatment radius, the overwhelming majority of these women have never had an implantable mesh placed. Chronic pelvic pain can occur with pelvic floor or levator ani spasm which commonly follows any type of vaginal surgery, including native tissue repairs.

Ultimately, the onus falls to the physician to make the final decision on whether or not they should be performing any pelvic organ prolapse procedure – whether mesh-augmented or not. The inherent risks of vaginal pain, vaginal scarring, dyspareunia, contraction and exposures of implantable material have been common knowledge among gynecologic and urologic surgeons for decades. The implementation of the use of mesh to augment prolapse repairs and decrease recurrences did not change that. Pelvic floor surgeons must rely on their education, training, review of the medical literature and most importantly their experience, knowledge, and skill as a surgeon in treating their patients.

In summary, there is an abundance of Level I evidence outlining the overall safety and efficacy of Gynemesh. The Prolift/Prolift+M (Gynemesh) system was a state-of-the-art, safe and effective product whose benefits in decreasing recurrence rates far outweighed the risk associated with its use.

I hold the above opinions to a reasonable degree of medical and scientific certainty. All opinions have been compiled based on my education, training and professional experience as a gynecologic surgeon. Additionally, I utilize my significant background in evaluating, diagnosing and treating women with pelvic floor pathologies, annual participation in national and international meetings on women's pelvic health, as well as an extensive review of the available medical literature as it pertains to prolapse treatment, including surgical and non-surgical strategies. I reserve my right to amend or supplement this opinion based on new information that becomes available.

C. Bryce Bowling, MD, FACOG, FPMRS, FACS
August 5, 2018